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L1: Entry 1 of 1

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TITLE: Regulated antigen delivery system (RADS)

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## INVENTOR-INFORMATION:

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## CLAIMS:

What is claimed is:

1. A microorganism comprising a regulated antigen delivery system (RADS), wherein the RADS comprises (a) a vector comprising (1) a gene encoding a desired gene product inserted into a site for insertion of a gene encoding a desired gene product, wherein the gene encoding the desired gene product is operably linked to a second control sequence; (2) a first origin of replication (ori) conferring vector replication using DNA polymerase III; and (3) a second ori conferring vector replication using DNA polymerase I, wherein the second ori is operably linked to a first control sequence repressible by a first repressor, and wherein the runaway vector does not comprise a phage lysis gene; and (b) a gene encoding a first repressor operably linked to a first activatable control sequence.

2. The microorganism of claim 1, wherein the first control sequence and the second control sequence are the same sequence.

3. The microorganism of claim 1, wherein the first control sequence and the second control sequence are different sequences.

4. The microorganism of claim 1, wherein the repressor is selected from the group consisting of LacI repressor and C2 repressor, and wherein the second control sequence is repressible by a second repressor.

5. The microorganism of claim 1, wherein (a) the vector is a plasmid; (b) the desired gene product is an antigen and (c) the microorganism is an attenuated bacterium.

6. The microorganism of claim 5, wherein the microorganism is a Salmonella sp.

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30-49

7. The microorganism of claim 5, wherein the first activatable control sequence is araCP.sub.BAD.
8. The microorganism of claim 5, further comprising an inactivating mutation in a native gene selected from the group consisting of cya, crp, phoPQ, opmR, galE, cdt, hemA, aroA, aroC, aroD and htrA.
9. The microorganism of claim 5, wherein the first ori is a pSC ori, and the second ori is a pUC ori.
10. The microorganism of claim 5, wherein the first control sequence is P22 P.sub.R and the first repressor is C2 repressor.
11. The microorganism of claim 5, wherein the second control sequence is P.sub.trc and wherein the second control sequence is repressible by a second repressor, and wherein the second repressor is a LacI repressor.
12. The microorganism of claim 11, wherein the first control sequence is P22 P.sub.R : the first repressor is C2 repressor; the first ori is a pSC ori, and the second ori is a pUC ori.
13. The microorganism of claim 12, wherein the vector is pMEG-771with a gene encoding an antigen.
14. The microorganism of claim 5, wherein the antigen is selected from the group consisting of Ery65 and SeM.
15. The microorganism of claim 5, wherein the desired gene product is operably linked to a eukaryotic control sequence.
16. The microorganism of claim 15, further comprising a .DELTA.endA mutation.
17. A runaway vector comprising the vector in the microorganism of claim 15.
18. The microorganism of claim 5, which exhibits delayed RADS characteristics, wherein the delayed RADS characteristics are conferred by an aeration selected from the group consisting of: mutations that delay the loss of activator molecules by metabolism and/or leakage, a mutation or insertion to increase repressor concentration, and inclusion of a vector control sequence with binding sites for more than one repressor and/or vector sequences encoding repressor molecules that act on a vector control sequence.
19. A vaccine for immunization of a vertebrate, the vaccine comprising the microorganism of claim 5, in a pharmaceutically acceptable carrier.
20. The vaccine of claim 19, wherein the microorganism is a Salmonella sp.
21. The vaccine of claim 19, wherein: (a) the first ori is a pSC ori; (b) the second ori is a pUC ori, which is operably linked to a repressing control sequence consisting of P22 P.sub.R ; (c) the product control sequence is P.sub.trc ; (d) a gene encoding a first repressor operably linked to a first inducible control sequence, wherein the first repressor is C2; and (e) a gene encoding a second repressor operably linked to a second inducible control sequence, wherein the second repressor is LacI.

22. The vaccine of claim 21, wherein the first activatable control sequence and the second inducible control sequence are both araCP.sub.BAD.

23. The vaccine of claim 22, wherein the microorganism further comprises an inactivating deletion in the araCBAD operon and or the areE gene.

24. A method of inducing immunoprotection in a vertebrate comprising administering the vaccine of claim 19 to the vertebrate.

[Previous Doc](#)

[Next Doc](#)

[Go to Doc#](#)